PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
KRISTINA BIEKER-BRADY
CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

REVIEWED BY FOREIGN FILING DEPT

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

	Date of mailing (*day/month/year*) 19 SEP 2005
Applicant's or agent's file reference 01948/098WO2	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US04/38865	International filing date (*day/month/year*) 19 November 2004 (19.11.2004)
Applicant BETH ISRAEL DEACONESS MEDICAL CENTER	

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19:
   The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

   When? The time limit for filing such amendments is normally two months from the date of transmittal of the international search report.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Facsimile No.: +41 22 740 14 35

   ACTION DUE Opt. Article 19
   DUE DATE 11.19.05
   INITIALS JPen

   For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders**

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase **until 30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer: Maria J Watson Marianne DiBrino, Ph.D. Telephone No. 571-272-1600

Form PCT/ISA/220 (January 2004) *(See notes on accompanying sheet)*

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 01948/098WO2	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. PCT/US04/38865	International filing date (*day/month/year*) 19 November 2004 (19.11.2004)	(Earliest) Priority Date (*day/month/year*) 19 November 2003 (19.11.2003)
Applicant BETH ISRAEL DEACONESS MEDICAL CENTER		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the Report**
   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      ☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box No. II)
3. ☐ **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      ☐ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☐ as selected by this Authority, because this figure better characterizes the invention.
   b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US04/38865

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : A61K 39/00, 45/00, 14/00
US CL : 424/185.1, 278.1; 514/350
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 424/185.1, 278.1; 514/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/36141 A2 (LYNCH et al) 10 May 2002, see entire document.	1-27, 29-35, 37, 39-46, 49-55 and 60-64
Y	US 6,433,147 B1 (NI et al). 13 August 2002 (13.08.2002), see entire document.	1-64
Y	US 5,846,827 A (CELIS et al) 08 December 1998 (08.12.1998), see entire document.	1-64

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search
10 June 2005 (10.06.2005)

Date of mailing of the international search report
19 SEP 2005

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (703) 305-3230

Authorized officer
~~Chan Y Christina~~
Marianne DiBrino
Telephone No. 703-308-0196

Form PCT/ISA/210 (second sheet) (January 2004)

Continuation of B. FIELDS SEARCHED Item 3:
WEST 2.2.2, STN(EMBASE, BIOSIS, MEDLINE, CAPLUS, SCISEARCH, PROMT, BIOBUSINESS)
search terms: inventors' names, mip-1a, mip-1 alpha, protein-1 alpha, mip-3a, mip-3 alpha, protein-3 alpha, fms-related protein tyrosine kinase 3 ligand, flt3l, cancer, tumor, autoimmune, immunogen, antigen, treat.

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
KRISTINA BIEKER-BRADY
CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	19 SEP 2005
Applicant's or agent's file reference 01948/098WO2	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/38865	19 November 2004 (19.11.2004)	19 November 2003 (19.11.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 39/00, 45/00, 14/00 and US Cl.: 424/185.1, 278.1; 514/350

Applicant

BETH ISRAEL DEACONESS MEDICAL CENTER

1. This opinion contains indications relating to the following items:

ACTION DUE Reply
DUE DATE 12.19.05
INITIALS JRM

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Marianne DiBrino, Ph.D. Telephone No. 571-272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/38865

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/38865

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	28, 36, 38, 47, 48, 56-59	YES
	Claims	1-27, 29-35, 37, 39-46, 49-55, 60-64	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-64	NO
Industrial applicability (IA)	Claims	1-64	YES
	Claims	NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

International application No.
PCT/US04/38865

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 28 objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because claim 28 is indefinite for the following reason(s): Claim 28 recites "said antigen" in line 1. There is insufficient antecedent basis for this limitation in the said claim.

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:
Claims 1-27, 29-35, 37, 39-46, 49-55, 60-64 lack novelty under PCT Article 33(2) as being anticipated by WO 02/36141 A2.

WO 02/36141 A2 teaches administering a combination of from two to five agents from the following: those that mobilize dendritic cells, stimulate maturation of dendritic cells, enhance an immune response of an effector T cell, or agents that cause death or growth inhibition of infectious agents (especially abstract). WO 02/36141 A2 teaches that induction of cell-mediated immune responses requires the interaction of at least three different types of cells: dendritic cells (DC), CD4+ Th cells and CD8+ effector T cells, or CTL (especially page 1 at paragraph 3). WO 02/36141 A2 teaches that an agent or more than one agent is administered to an individual human including an infant afflicted with or at risk for a condition characterized by the presence of a pathogenic or opportunistic organism(s), said agent being a DC mobilization factor such as human or murine Flt3L or biologically active fragments thereof and/or GM-CSF, a chemoattractant(s) to attract the mobilized DC such as MIP-1a and/or MIP-3a, along with one or more antigens, said antigens may be HIV antigens, other viral antigens, bacteria, yeast, fungi and protozoa, or viruses that cause cancer or demyelinating autoimmune diseases. WO 02/36141 A2 teaches that the various agents may be administered locally in or near a site of infection or systemically. WO 02/36141 A2 teaches that the agents may be administered to humans in a variety of administration forms and dosages or by using vectors or naked DNA in gene therapy techniques. WO 02/36141 A2 teaches optionally administering a second anti-microbial or anti-viral therapy. WO 02/36141 A2 teaches administering a second therapeutic regimen within 1 to 25 days after the first. WO 02/36141 A2 teaches that those of ordinary skill in the art are able to optimize the order and/or timing of the steps, as well as the dosages and routes of administration by routine experimentation (especially page 2 at the first two paragraphs, page 10 at paragraph 2, page 11 at paragraphs 1 and 3, page 18 at paragraphs 2 and 3, pages 20-23, claims, Figure 1, page 5 at paragraph 1, pages 6-page 9 at paragraph 2).

Claims 7, 8 and 60 are included in this rejection because the art method appears to be the same or similar absent a showing of unobvious differences, i.e., with respect to the degree of augmentation of the T cell response recited in the said claims. Claim 18 is included in this rejection because injection into the same injection site meets the claim limitation of "within no more than 20 cm apart".

Claim 27 and 37 are included in this rejection because the antigen is the same antigen present in the infection or the tumor. Claim 21 is included because the art method inherently prevents viral transmission in an infant that is breastfeeding. Claim 39 is included in this rejection because the art method appears to be the same or similar to the claimed method since the method improves immune response, less vaccine would be required.

Claims 1-64 lack an inventive step under PCT Article 33(3) as being obvious over WO 02/36141 A2 in view of US 6,433,147 B1 and US 5,846,827 A.

WO 02/36141 A2 teaches administering a combination of from two to five agents from the following: those that mobilize dendritic cells, stimulate maturation of dendritic cells, enhance an immune response of an effector T cell, or agents that cause death or growth inhibition of infectious agents (especially abstract). WO 02/36141 A2 teaches that induction of cell-mediated immune responses requires the interaction of at least three different types of cells: dendritic cells (DC), CD4+ Th cells and CD8+ effector T cells, or CTL (especially page 1 at paragraph 3). WO 02/36141 A2 teaches that an agent or more than one agent is administered to an individual human including

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

an infant afflicted with or at risk for a condition characterized by the presence of a pathogenic or opportunistic organism(s), said agent being a DC mobilization factor such as human or murine Flt3L or biologically active fragments thereof and/or GM-CSF, a chemoattractant(s) to attract the mobilized DC such as MIP-1a and/or MIP-3a, along with one or more antigens, said antigens may be HIV antigens, other viral antigens, bacteria, yeast, fungi and protozoa, or viruses that cause cancer or demyelinating autoimmune diseases. WO 02/36141 A2 teaches that the various agents may be administered locally in or near a site of infection or systemically. WO 02/36141 A2 teaches that the agents may be administered to humans in a variety of administration forms and dosages or by using vectors or naked DNA in gene therapy techniques. WO 02/36141 A2 teaches optionally administering a second anti-microbial or anti-viral therapy. WO 02/36141 A2 teaches administering a second therapeutic regimen within 1 to 25 days after the first. WO 02/36141 A2 teaches that those of ordinary skill in the art are able to optimize the order and/or timing of the steps, as well as the dosages and routes of administration by routine experimentation (especially page 2 at the first two paragraphs, page 10 at paragraph 2, page 11 at paragraphs 1 and 3, page 18 at paragraphs 2 and 3, pages 20-23, claims, Figure 1, page 5 at paragraph 1, pages 6-page 9 at paragraph 2).

WO 02/36141 A2 does not teach wherein viral vector is adenovirus or a poxvirus or fowl poxvirus, nor wherein at least 0.2 ug of vector is provided, nor wherein the antigen is an immunogenic peptide from HIV pol, nor wherein the cancer is melanoma, nor wherein the antigen is from MAGE-3.

US 6,433,147 B1 discloses using viral vectors comprising promoters such as adenovirus, fowl pox viruses or pox viruses in general for expression of polypeptides, in mammalian host cells, or alternately, use of naked DNA or RNA encoding a polypeptide in the dosage of from about 0.05 ug/kg body weight(especially columns 32-34, Example 28).

US 5,846,827 A discloses immunogenic peptides from HIV pol and MAGE-3 expressed on melanoma cancer cells

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used a viral vector that is adenovirus or a poxvirus or fowl poxvirus as disclosed in US 6,433,147 B1 as the vector taught in the method of WO 02/36141 A2.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in because WO 02/36141 A2 teaches using a vector for nucleic acid administration in the method and US 6,433,147 B1 discloses suitable vectors for expression of polypeptides in mammalian cells.

Claims 48 and 59 are included in this rejection because it would have been obvious to use at least the same amount of vector comprising DNA as the amount disclosed by US 6,433,147 B1 for naked DNA administration because the vector comprising DNA has less DNA per dosage weight than does naked DNA.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used an immunogen from HIV pol antigen disclosed by US 5,846,827 A to treat viral infection such as HIV taught by WO 02/36141 A2, or the MAGE-3 immunogenic peptide to treat melanoma disclosed by US 5,846,827 using the method taught by WO 02/36141 A2, but rather to treat cancer that is non-virally induced.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to enhance an immune response in HIV infection or cancer, because WO 02/36141 A2 teaches a method for enhancing immune response in cancer or viral infection comprising administering immunogenic peptides, and US 5,846,827 A discloses immunogenic peptides from HIV pol and MAGE-3 expressed on melanoma cancer cells.

Claims 1-64 meet the criteria set out in PCT Article 33(4), and thus meet industrial applicability because the subject matter claimed can be made or used in industry.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1 [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2 [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3 [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." **or**
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4 [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted; the applicant must preferably, at the time of filing, the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated elected Office, see the *PCT Applicant's Guide*, Volume II.